Tetrahedron Letters No.22, pp. 1803-1804, 1969. Pergamon Press. Printed in Great Britain.

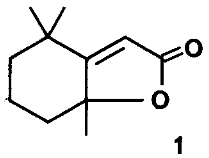
SYNTHESIS OF THEASPIRONE

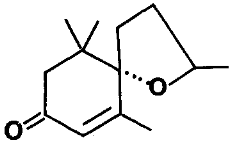
Aiya Sato and Hiroshi Mishima

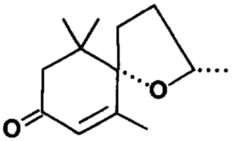
(Central Research Laboratories, Sankyo Co. Ltd., Tokyo)

(Received in Japan 22 March 1969; received in UK for publication 8 April 1969)

A vast number of investigations on the volatile fraction of black tea have been directed toward the detection of substances which play an important role in tea flavor. More recently discovered are two compounds, 2-hydroxy-2,2,6-trimethylcyclohexylidene acetic acid lactone (1)[1] and 1-oxa-8-oxo-2,6,10,10-tetramethyl-spiro[4,5]-6-decene (2a or 2b)[2]. The latter was named theaspirone by Ina et al[2]. They stated that a very dilute solution of these two compounds in an appropriate ratio has a fragrant tea odor.


1

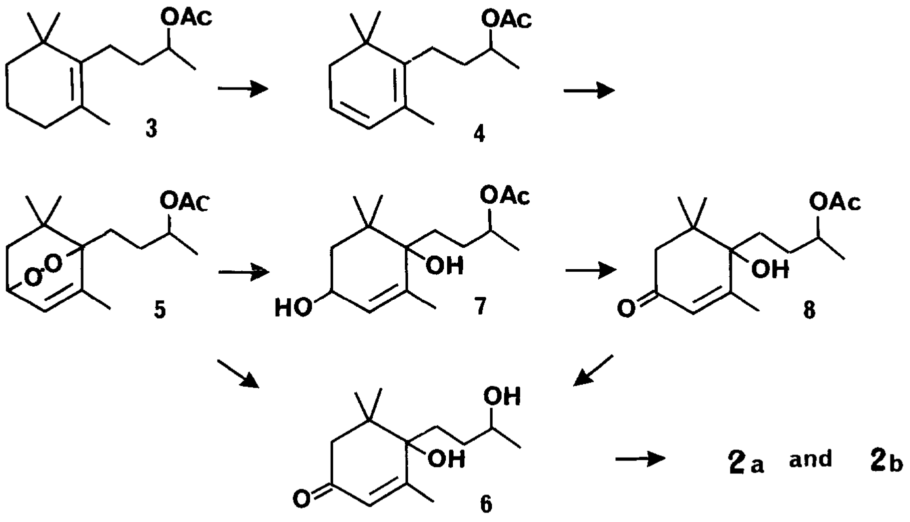

2a


2b

Dihydro-β-ionol acetate (3)[3] was smoothly transformed to the conjugated diene (4) by bromination with N-bromosuccinimide and successive treatment with dimethylaniline. The UV spectrum of 4 shows absorption maxima at 242, 250, and 263 mμ (ε 4,200, 4,400, and 4,600 respectively) in agreement with a cis conjugated diene.

Photo-oxidation of 4 in the presence of eosine in ethanol afforded an peroxide (5), the structure of which was confirmed by NMR spectrum. Catalytic reduction of the peroxide (5) with Lindlar's catalyst afforded a diol (7), m.p. 115°, which was oxidized to a ketone (6), IR $\nu_{C=C}$ 1660 cm^{-1}; UV λ_{max}^{EtOH} 243 mμ (ε 9,900), with manganese dioxide. This ketone (6) was also prepared by the treatment of 5 with sodium hydroxide.

Ether cyclization was effected by heating a dimethylsulfoxide solution of 6. Although the resulting ether formed a crystalline semicarbazone, m.p. 208-9°, the ether regenerated from the semicarbazone was shown to be a mixture (approximate ratio 1:1) of two racemic stereoisomers (2a and 2b) by gas chromatography (diethylene glycol succinate ester). The separation of the isomers was carried out by gas-phase chromatography.



The spectral data (IR, UV, MS, NMR) of two racemic stereoisomers are almost superimposable and there are no noticeable differences between them. The spectral data of theaspirone coincide with those of synthetic one. The problem of the stereochemistry of theaspirone remains unsolved.

References

1) Isolation: J. Bricout, R. Viani, F. Müggler-Chavan, J. P. Marion, D. Reymond, and R. H. Egli, Helv. chim. Acta, 50, 1517 (1967). Synthesis: T. Sakan, S. Isoe, and S. B. Hyeon, Tetrahedron Letters, 1623 (1967); E. Demole and P. Enggist, Helv. chim. Acta, 51, 481 (1968).

2) K. Ina, Y. Sakato, and H. Fukami, Tetrahedron Letters, 2777 (1968).

3) Y. R. Naves and P. Bachmann, Helv. chim. Acta, 26, 2151 (1943).